UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/923,752	09/16/97	PAPADOPOULOU	B 1038-729M18

EXAMINER

HM21/1124

MASCIOLI, K

ART UNIT	PAPER NUMBER
1645	7

SIM & MCBURNEY
330 UNIVERSITY AVENUE
6TH FLOOR
TORONTO ON M5T 1R7
CANADA

AIR MAIL

DATE MAILED: 11/24/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on Sept 24, 98 (Paper No. 6)

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire Three month(s), ~~or thirty days,~~ whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-20 is/are pending in the application.
Of the above, claim(s) 17-20 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1-16 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☒ Claim(s) 1-20 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). 5
☐ Interview Summary, PTO-413
☒ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

* U.S. GPO: 1998-421-533/40206

DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1645.

1. Applicant's election with traverse of Group I, claims 1-16 in paper no. 6 filed 9/28/98 is acknowledged. Claims 1-20 are pending in the application. The traversal is on the ground(s) that claims grouped separately are interrelated and should be examined together. These arguments have been fully considered but are not found to be persuasive. MPEP 803 states that restriction is proper between patentably distinct inventions, where the inventions are independent or distinct as claimed and there is serious burden on the examiner if restriction is not required. The term "distinct" is defined to mean that two or more subjects as disclosed are related, for example, as product and method of use, etc., but are capable of separate manufacture, use or sale as claimed, and are patentable over each other. In the instant situation, the inventions of Groups I-III are drawn to distinct inventions which are related as separate products and methods capable of separate manufacture, use or sale as described in the previous office action. Restrictions between the inventions is deemed to be proper for the reasons previously set forth. A burden exists in the examination of these inventions. MPEP 803 states that a burden can be shown if the examiner shows either separate classification, separate status in the art or a different field of search. In the instant case a burden has been established in showing that the inventions of Groups I-III are

classified separately necessitating different searches in the U.S. Patent shoes. Additionally, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Further, it is submitted that the inventions of Groups I-III have acquired a separate status in the art. Clearly different searches and issues are involved in the examination of each group. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claims 17-20 are withdrawn from consideration as being non-elected invention.

Accordingly claims 1-16 are being examined herewith.

2. Claim 12 is rejected under 35 USC 112, second paragraph, because the term "said infection" lacks antecedent basis.

3. Claims 1-6 and 11-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for plasmids pneo-mGM CSF and pneo-hGM and parasites *Leishmania donovani* and *Leishmania major*, does not reasonably provide enablement for a broadly claimed a macrophage infecting parasite, genus Leishmania expressing a GM-CSF gene, immunogenic composition, and generating a protective immune response against a disease caused by a macrophage infecting parasite. The specification does not reasonably provide enablement for a macrophage infecting parasite GM-CSF polypeptide which includes a large number of

polypeptides having different structural and biological activities of unknown nature from an indeterminate number of parasites and, an additional cytokine further broaden the scope of the claims, from only one example of the specification represented as figure no. 1, it is unknown and unpredictable as to how fig no. 1 Constructs would compare with other growth factors and cytokines in terms of structural and biological activities. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. One cannot apply the teaching of specification from one example to get other variants, in the absence of such information one of skill in the art would not be able to obtain, or predict how to modify and retain the structural and biological properties of, all of the GM-CSF of indeterminate number of parasites encompassed in the claims without undue experimentation. It is suggested the claims should be directed to enabled constructs of figure 1. Claims 11-16 are further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims are drawn to a "an immunogenic composition" comprising an attenuated form of said parasite to treat and protect against *Leishmania* infection. The use of such a composition and/or a vaccine is highly unpredictable and experimental. Weiser et al teaches that it is not yet clear how GM-CSF induces antileishmanial activity in macrophages upon infection with leishmania (see page 1443, para 3). Homogenous human rGM-CSF devoid of other lymphokines induces intracellular killing of *L. Donovani* by monocyte-derived macrophages. The

role of GM-CSF in vivo as a macrophage-activating factor and its functional relationship to cytokine such as IFN-γ remains to be determined. Simultaneous administration of suboptimal doses of rGM-CSF and IFN-γ to macrophages results in greater antileishmanial activity by these cells than the administration of either lymphokine alone, although no enhancement of antileishmanial activity is observed when optimal doses of these lymphokines are applied together. The complexity and unpredictability of the art to which invention pertains provides reasonable basis to question as to the accuracy of applicants's assertion that the claimed immunogenic composition and/or vaccine can be used for protection of leishmania disease in human. The specification provides no evidence which would allow one to predict that the claimed composition can be effectively used for the treatment of immunogenic composition and/or vaccine can be used for protection of leishmania. The specification does not set forth sufficient teachings to allow one skilled in the art to use the claimed composition.

4. ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, and 10 are rejected under 35 U.S.C. 102 (b)as being anticipated by Moore et al (J. Immunol. 1994, 152: 2930-2937).

Moore et al disclose a macrophage infecting parasite such as Leishmania expressing a granulocyte macrophage colony stimulating factor (GM-CSF) and additional cytokine e.g., IL-6 (see abstract, page 2933 para 2-3 and entire document).

5.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 5-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moore et al as applied to claims 1-4, and 10 above, and further in view of Wong et al (Science 1985 228: 810-815).

The teachings of Moore et al is set forth above which teaches a macrophage infecting parasite such as Leishmania expressing a granulocyte macrophage colony stimulating factor (GM-CSF) and additional cytokine e.g., IL-6 (see abstract, page 2933 para 2-3 and entire document). Moore et al does not specifically teach term human and murine GM-CSF gene.

Wong et al teaches human and murine GM-CSF gene (See abstract , lines 6-8).

It would have been obvious to one of ordinary skill in the art at the time of invention was made to isolate a macrophage infecting parasite expressing a GM-CSF gene of L. donovani (infects human) as set forth by Moore et al and isolate a macrophage infecting parasite expressing a GM-CSF gene from human and murine origin as set forth by Wong et al. One would have been motivated to do so because the isolation of a macrophage infecting parasite expressing a GM-CSF gene from one source to another i.e., human/murine, which is within the level of one of ordinary skill in the art and routinely used. The invention as a whole is prima facie obvious.

6. Claims 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moore et al in view of Wong et al and further in view of Laban et al (Nature 1990 Vol. 343: 572-574).

The teachings of Moore et al and Wong et al are set forth above.

Moore et al disclose a macrophage infecting parasite such as Leishmania expressing a granulocyte macrophage colony stimulating factor (GM-CSF) and additional cytokine e.g., IL-6 (see abstract, page 2933 para 2-3 and entire document).

Wong et al teaches human and murine GM-CSF gene (See abstract , lines 6-8).

Laban et al teaches the expression of neomycin gene using the -tubulin intergenic sequences of Leishmania enrietti (see abstract, lines 6-10 and entire document).

It would have been obvious to one of ordinary skill in the art at the time of invention was made to isolate a macrophage infecting parasite expressing a GM-CSF gene of L. donovani (infects human) as set forth by Moore et al and isolate a macrophage infecting parasite expressing a GM-CSF gene from human and murine origin as set forth by Wong et al. One would have been motivated to do so because the isolation of a macrophage infecting parasite expressing a GM-CSF gene from one source to another i.e., human/murine, which is within the level of one of ordinary skill in the art and routinely used. It would have been further obvious to one of ordinary skill in the art at the time of invention was made to express GM-CSF gene simply by substituting neomycin gene of Laban et al. One would be motivated to do so because Laban et al teaches stable expression of the genes rather than transient expression that has the advantage for further studies of parasitic diseases. The invention as a whole is a prima facie obvious over combination of cited references.

7. Claims 9 and 11-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moore et al in view of Maltashewski et al (WO 95/06729 9 March 1995).

The teachings of Moore et al is set forth above.

Maltashewski et al teaches differential expression of *Leishmania* genes and proteins that have utility as vaccines, diagnostic reagents and tools for the generation of immunological

reagents and the generation of attenuated variants of *Leishmania* (see abstract, pages 31-32, claims 19 and 24-29).

It would have been obvious to one of ordinary skill in the art at the time of invention was made to and isolate a macrophage infecting parasite expressing a GM-CSF gene as set forth by Moore et al and functionally disable the virulent gene of the parasite and use attenuated form of said parasite as immunogenic composition and/or vaccine to treat and protect *Leishmania* infection in a host as suggested by Maltashewski et al. One would have been motivated to do so because such an immunogenic composition would be useful to treat said disease as suggested by Maltashewski et al. The invention as a whole is prima facie obvious.

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 1-6 and 10 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter i.e., reads on a naturally occurring a macrophage infecting parasite expressing a GM-CSF gene, and cytokine which is a product of nature.

7. Double Patenting:

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See

Miller v. Eagle Mfg. Co., 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-16 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-16 of copending Application No. 08/713,768. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khalid Masood whose telephone number is (703) 305-6998.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 180 by facsimile transmission via the PTO Fax Center, located in Crystal Mall 1. The Fax Center number is (703) 308-4242. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

If attempts to reach the examiner by telephone are unsuccessful, the examiners's supervisor, Dr. Anthony Caputa, can be reached on (703)308-3995.

ANTHONY C. CAPUTA
PRIMARY EXAMINER

Khalid Masood, Ph.D.
November 20, 1998